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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,868	05/04/2001	Patrick L. Iversen	0450-0037.30	8375

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EXAMINER

LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 08/26/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/848,868	Applicant(s) IVERSEN ET AL.	
	Examiner Karen A. Lacourciere	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 05 June 2003.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-22 and 34-37 is/are pending in the application.

4a) Of the above claim(s) 8-17, 19-22 and 34-37 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-7 is/are rejected.

7) ☒ Claim(s) 18 is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Election/Restrictions

Claims 8-17, 19-22 and 34-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

This application contains claims 8-17, 19-22 and 34-37 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 -7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite because it appears to contain two separate sentences and, therefore, it is unclear what is part of the actual claimed subject matter, specifically, the claim ends in a period and is then followed by a figure. Further, the claim is indefinite because the claim includes a limitation "as shown below". It is unclear what "below" is referring to, for example, does this phrase make reference to generally any of the any of

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the following claims? Claims 3-7 are indefinite for the same reasons due to dependence on claim 2.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are maintained as rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO: 35 and 36 which correspond to antisense complementary to a target region of a nucleic acid encoding p53 wherein the 5' end of the target region is 1-25 bases downstream of a splice acceptor site at the exon 2 splice junction of human p53. SEQ ID NO: 35 and 36 meet the written description provisions of 35 USC 112, first paragraph. However, claims 1-7 are directed to encompass antisense complementary to a target region wherein the 5' end of the target region is 1-25 bases downstream of any normal splice acceptor site, which would include cryptic splice sites. Antisense complementary to these target regions do not meet the written description provision of 35 USC 112, first paragraph. The specification provides consensus sequence to identify splice acceptor sites in yeast and human RNA

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(see page 11), however, these consensus sequences are not absolute, for example, the mammalian consensus sequence has one invariable A residue at the branch point, an AG site located at a variable length from the A and all other residues are only vaguely defined. The yeast consensus is more well defined, but still highly variable. The specification has defined the sequence of one target region (SEQ ID NO:36) at one splice acceptor site in one p53 mRNA, but has not provided the location of other splice acceptor sites, or the structure (ie. sequence) of the down stream target region of such sites. The skilled artisan would not recognize that the inventors had possession of antisense targeted to other downstream regions within the human p53 mRNA, or to regions downstream of acceptor sites within other p53 mRNA's, because the specification does not describe the location and sequence of the splice acceptor sites within these mRNA. The consensus sequences are not sufficient to describe these acceptor sites because the consensus sequences are vague and highly variable. The specification has not described which sites within p53 mRNA's fit these consensus sequences and actually act as splice acceptors. The specification provides insufficient written description to support the genus encompassed by the claim, because the claims antisense encompass a broad genus of sequences, targeted to regions throughout nucleic acids encoding p53, with variable sequences, targeted to splice acceptors sites which are also highly variable.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 35 and 36, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required.

Therefore, only SEQ ID NO: 35 and 36 but not the full breadth of the claim meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Response to Arguments

Applicant's arguments filed June 5, 2003 have been fully considered but they are not persuasive.

In response to the rejection of record of claim 1-7 under 35 USC 112, first paragraph, written description, Applicant argues that the claims are limited to locations 1-25 bases downstream of "normal" splice acceptor sites in human p53 and, that the normal splice acceptor sites were well known in the art at the time of filing. Applicant argues Genbank provides normal splice acceptor sites for human p53 and that the specification provides such sites in the table on page 35.

These arguments have not been found to be persuasive because the term "normal splice acceptor site" would also encompass normal cryptic sites within the

human p53 gene, which are not defined in the specification and, further, are not defined in the art, including within human p53 genes in Genbank, including in Genbank Accession number X54156. Applicant points to the table on page 35 of the specification, however, this table only defines two sites, those targeted by SEQ ID NO:35 and 36, and does not provide written description for a sufficient number of species within the genus to provide written description for the full genus.

Allowable Subject Matter

Claim 18 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. A morpholino oligonucleotide consisting of SEQ ID NO: 35 is free of the prior art and would be useful to inhibit the expression of p53 in a cell in culture, for example, possibly acting as a traditional antisense.

Conclusion

Any rejection of record not repeated herein is considered to be withdrawn.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Thursday 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
August 25, 2003


KAREN LACOURCIERE
PATENT EXAMINER